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ning of each regular issue of the PCT Gazette.*

(54) Title: IRS MODULATORS

(57) Abstract: This invention is directed to a general method for the chronic treatment, potential cure, or prevention of various metabolic and related diseases in people, including diabetes, by modulating IRS2 activity in cells and tissues in the body. IRS1 and IRS2 are part of the insulin or insulin-like growth factor signaling pathway. By upregulating the levels or functional activity of IRS2, insuling is used more efficiently by the body to control nutrient levels. By upregulating IRS2 levels or functional activity in pancreatic  $\beta$ -cells, glucose sensing and insulin secretion are enhanced.

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/41745

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61P 5/00; C12Q 1/68

US CL : 514/2; 435/6

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/2; 435/6

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Dachicourt et al. Glucagon-like peptide-1(7-36)-amide confers glucose sensitivity to previously glucose-incompetent beta-cells in diabetic rats: in vivo and in vitro studies. J. of Endo. 1997. Vol 155: pp. 369-376, esp. p. 375: paragraph 3 and 4.	1-6 and 9-15
X,P	Drucker, DJ, Development of Glucagon-like Peptide-1-Based Pharmaceuticals as Therapeutic Agents for the Treatment of Diabetes, Current Pharmaceutical Design 2001, Vol 1: pp. 1399-1412, esp. p. 1400: Figure 1.	1-6 and 8-15
Y	Trumper et al., Inegrative Mitogenic Role of Protein Kinase B/Akt in Beta-Cells, Ann. NY Acad. Sci. 2000, Vol. 921: pp. 242-250, esp. p. 244-245.	1-15
X	US 5,858,701 (White et al.) 19 Jan. 1999 (19.01.1999), Column 4: lines 45-54, Column 6: lines 39-57, Column 8: lines 26-32.	16-17



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